

WHAT IS CLAIMED IS:

1. An agent which influences the partitioning of dietary lipids between the liver and peripheral tissues for use as a medicament.
2. The agent of Claim 1 for use in treating a condition in which it is desirable to increase the partitioning of dietary lipids to the liver, reducing food intake in obese individuals, reducing the levels of free fatty acids in obese individuals, decreasing the body weight of obese individuals, or treating an obesity related condition selected from the group consisting of obesity-related atherosclerosis, obesity-related insulin resistance, obesity-related hypertension, microangiopathic lesions resulting from obesity-related Type II diabetes, ocular lesions caused by microangiopathy in obese individuals with Type II diabetes, and renal lesions caused by microangiopathy in obese individuals with Type II diabetes.
3. The agent of Claim 1, wherein said agent is selected from the group consisting of AdipoQ analogs, AdipoQ homologs, AdipoQ derivatives, and fragments of any of the preceding agents.
4. The agent of Claim 1, wherein said agent comprises an LSR antagonist or an LSR agonist.
5. A polypeptide comprising a consensus sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:2 for use as a medicament.
6. A polypeptide comprising an amino acid sequence selected from the group consisting of polypeptides having at least 25% homology to one of the sequences of SEQ ID NOs.: 7-14, polypeptides having at least 50% homology to one of the sequences of SEQ ID NOs.: 7-14, and polypeptides having at least 80% homology to one of the sequences of SEQ ID NOs: 7-14 for use as a medicament.
7. A C1q polypeptide, derivative, homologue or a fragment of any of the preceding compounds for use as a medicament.
8. An AdipoQ polypeptide or a derivative or homologue thereof or a fragment thereof for use as a medicament.
9. An ApM1 polypeptide or a derivative or homologue thereof or a fragment thereof for use as a medicament.
10. Use of a compound that influences the partitioning of dietary lipids between the liver and peripheral tissues in the manufacture of a medicament for treating a condition in which the partitioning of dietary lipids to the liver is abnormal.
11. The use of Claim 10 wherein said medicament is for reducing food intake in obese individuals, reducing the levels of free fatty acids in obese individuals, decreasing the body weight of obese individuals, or treating an obesity related condition selected from the group consisting of obesity-related atherosclerosis, obesity-related insulin resistance, obesity-related hypertension, microangiopathic lesions resulting from obesity-related Type II diabetes, ocular lesions caused by microangiopathy in obese individuals with Type II diabetes, and renal lesions caused by microangiopathy in obese individuals with Type II diabetes.
12. The use of Claim 10, wherein said compound is selected from the group consisting of AdipoQ analogs, AdipoQ homologs, AdipoQ derivatives, and fragments of any of the preceding agents.

13. The use of Claim 10, wherein said compound is an agonist or antagonist of the Lipolysis Stimulated Receptor.

14. The use of Claim 10, wherein said compound comprises an amino acid sequence selected from the group consisting of polypeptides having at least 25% homology to one of the sequences of SEQ ID NOs.: 7-14, polypeptides having at least 50% homology to one of the sequences of SEQ ID NOs.: 7-14, and polypeptides having at least 80% homology to one of the sequences of SEQ ID NOs.: 7-14 for use as a medicament.

15. The use of Claim 10, wherein said compound is a polypeptide that specifically binds a γ subunit of the Lipolysis Stimulated Receptor or a gC1q-R or a gC1q-R homologue, and wherein said compound is not a subunit of the Lipolysis Stimulated Receptor.

16. The use of Claim 15, wherein said compound comprises a polypeptide selected from the group consisting of C1q, AdipoQ, ApM1, Acrp 30, cerebellin, multimerin and fragments of any of these polypeptides.

17. Use of a polypeptide having binding specificity for a γ subunit of the Lipolysis Stimulated Receptor or a gC1q-R or a gC1q-R homologue for treatment of obesity, wherein said polypeptide is not a subunit of the Lipolysis Stimulated Receptor.

18. The use of Claim 10, wherein said polypeptide is selected from the group consisting of polypeptides having about 25% homology to an ApM1 protein, polypeptides having about 50% homology to an ApM1 protein and polypeptides having about 80% homology to an ApM1 protein.

19. The use of Claim 10, wherein said polypeptide is selected from the group consisting of C1q, AdipoQ, ApM1, Acrp 30, cerebellin, multimerin and fragments of any of these polypeptides.

20. The use of Claim 10, wherein said polypeptide is a human polypeptide.

21. The use of Claim 20, wherein said human polypeptide is selected from the group consisting of ApM1 and fragments of ApM1.

22. A polypeptide that specifically binds the gC1q-R protein for use in the treatment of obesity, wherein said polypeptide is not a subunit of the Lipolysis Stimulated Receptor.

23. The polypeptide of Claim 22, selected from the group consisting of C1q, AdipoQ, ApM1, Acrp 30, cerebellin and multimerin.

24. A composition for modulating activity of the Lipolysis Stimulated Receptor, comprising:
a compound having binding specificity for the gC1q-R protein, wherein said compound is not a subunit of the Lipolysis Stimulated Receptor; and
a pharmaceutically acceptable carrier.

25. A composition for modulating activity of the Lipolysis Stimulated Receptor, comprising:
a polypeptide comprising an amino acid sequence being at least 25% homologous to a sequence selected from the group consisting of any one of SEQ ID NOs 7-14; and
a pharmaceutically acceptable carrier.

26. A composition for modulating activity of the Lipolysis Stimulated Receptor, comprising:
a polypeptide comprising a consensus sequence selected from the group consisting of SEQ ID

NO:1 and SEQ ID NO:2; and

a pharmaceutically acceptable carrier.

27. A method of reducing plasma lipoprotein levels in an animal, comprising the steps of:

identifying an animal having a measurable plasma lipoprotein level;

5 administering to said animal a composition that includes a pharmaceutically acceptable carrier and a polypeptide that is at least 25% homologous to an ApM1 protein; and

allowing passage of a period of time to permit reduction in said measurable plasma lipoprotein level.

28. The method of Claim 27, wherein said animal is a mammal.

10 29. The method of Claim 28, wherein the administering step comprises injecting the pharmaceutical composition.

30. The method of Claim 29, wherein the pharmaceutical composition is injected intravenously.

31. The method of Claim 27, wherein the administering step comprises implanting surgically an infusion device for releasing the pharmaceutical composition.

15 32. A method of identifying candidate pharmaceutical agents for reducing plasma triglyceride levels in an animal, comprising the steps of:

identifying a compound that comprises a consensus sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:2;

obtaining a test animal having an initial level of plasma triglycerides;

20 administering said compound to the test animal;

waiting for a period of time;

measuring a post-treatment level of plasma triglycerides in a blood sample obtained from the test animal; and

25 identifying as candidate pharmaceutical agents any compound that results in a post-treatment level of plasma triglycerides that is lower than said initial level.

33. The method of Claim 32, wherein the test animal is a mammal.

34. The method of Claim 33, further comprising the step of feeding a high-fat meal to the mammal.

35. The method of Claim 34, wherein the high-fat meal includes about 60% fat, about 20% protein, and about 20% carbohydrate, and wherein said 60% fat comprises about 37% saturated fatty acids, about 36% polyunsaturated fatty acids and about 36% polyunsaturated fatty acids.

36. A method for treating an animal having a condition in which it is desirable to increase the partitioning of dietary lipids to the liver, comprising the step of administering an LSR agonist to the animal having said condition.

37. A method for treating an animal having a condition in which it is desirable to decrease the partitioning of dietary lipids to the liver, comprising the step of administering an LSR antagonist to the animal having said condition.

38. An agent which increases the activity of a compound which increases the partitioning of dietary lipids to the liver for use as a pharmaceutical.

39. The agent of Claims 38, for use in reducing food intake in obese individuals, reducing the levels of free fatty acids in obese individuals, decreasing the body weight of obese individuals, or treating an obesity related condition selected from the group consisting of obesity-related atherosclerosis, obesity-related insulin resistance, obesity-related hypertension, microangiopathic lesions resulting from obesity-related Type II diabetes, ocular lesions caused by microangiopathy in obese subjects with Type II diabetes, and renal lesions caused by microangiopathy in obese subjects with Type II diabetes.

40. The agent of Claim 38, wherein said agent increases the activity of adipoQ, ApM1, a compound analogous to adipoQ or ApM1, or the LSR receptor.

41. The agent of Claim 38, wherein said agent is selected from the group consisting of derivatives of adipoQ, ApM1, C1q, derivatives of a compound analogous to any of the preceding compounds wherein said derivatives exhibit greater activity than the corresponding wild type protein and antibodies capable of specifically binding the γ subunit, the C1q receptor (gC1q-R) or a protein related thereto.

42. The agent of Claim 38, wherein said agent is selected from the group consisting of derivatives of compounds comprising at least one of the sequences of SEQ ID NOs.: 1 and 2, derivatives of compounds comprising an amino acid sequence having at least 25% homology to a sequence selected from the group consisting of SEQ ID NOs. 7-14, derivatives of compounds comprising an amino acid sequence having at least 50% homology to a sequence selected from the group consisting of SEQ ID NOs. 7-14, and derivatives of compounds comprising an amino acid sequence having at least 80% homology to a sequence selected from the group consisting of SEQ ID NOs. 7-14, wherein said derivatives exhibit greater activity than the corresponding wild type protein.

43. The agent of Claim 38, wherein said agent comprises a nucleic acid encoding a polypeptide or protein which influences the partitioning of dietary lipids between the liver and peripheral tissues for use as a medicament.

44. The agent of Claim 43, wherein said nucleic acid encodes a protein or polypeptide selected from the group consisting of adipoQ, ApM1, C1q, polypeptides analogous to ApM1, polypeptides having at least one of the consensus sequences of SEQ ID NO: 1 and SEQ ID NO: 2, analogs of any of the preceding polypeptides, homologs of any of the preceding polypeptides, derivatives of any of the preceding polypeptides, and fragments of any of the preceding polypeptides.

45. The agent of Claim 43, wherein said nucleic acid encodes a polypeptide selected from the group consisting of polypeptides comprising an amino acid sequence having at least 25% homology to one of the sequences of SEQ ID NOs.: 7-14, polypeptides comprising an amino acid sequence having at least 50% homology to one of the sequences of SEQ ID NOs.: 7-14, and polypeptides comprising an amino acid sequence having at least 80% homology to one of the sequences of SEQ ID NOs.: 7-14.

46. The agent of Claim 38, wherein said agent is selected from the group consisting of small molecules and drugs.

47. The agent of Claim 38, wherein said agent is for administration to an individual having a below normal level of activity of adipoQ, ApM1, or an analogous protein.

48. An agent which decreases the activity of a compound which increases the partitioning of dietary lipids to the liver for use as a pharmaceutical.

5 49. The agent of Claim 48, for use in treating cachexia in subjects with neoplastic or para-neoplastic syndrome or eating disorders.

50. The agent of Claim 48, wherein said agent decreases the activity of adipoQ, ApM1, a compound analogous to adipoQ or ApM1, or the LSR receptor.

10 51. The agent of Claim 48, wherein said agent is an antibody which binds a compound selected from the group consisting of adipoQ, ApM1, C1q, a protein analogous to any of the preceding proteins, a derivative of adipoQ, C1qa, C1qb, C1qc, mul, cer, ApM1, or acrp which inhibits the activity of wild type adipoQ or wild type ApM1, fragments of any of the preceding polypeptides, the γ subunit, the C1q receptor (gC1q-R) or a protein related thereto.

15 52. The agent of Claim 48, wherein said agent is an antibody which binds a polypeptide selected from the group consisting of polypeptides comprising at least one of the sequences of SEQ ID NOs: 1 and 2, polypeptides comprising an amino acid sequence having at least 25% homology to a sequence selected from the group consisting of SEQ ID NOs. 7-14, polypeptides comprising an amino acid sequence having at least 50% homology to a sequence selected from the group consisting of SEQ ID NOs. 7-14, and polypeptides comprising an amino acid sequence having at least 80% homology to a sequence selected from the group consisting of SEQ ID NOs. 7-14.

20 53. The agent of Claim 48, wherein said agent is selected from the group consisting of antisense nucleic acids to the adipoQ gene, the ApM1 gene or a portion thereof and nucleic acids capable of forming a triple helix with a portion of the adipoQ gene or the ApM1 gene.

25 54. The agent of Claim 48, wherein said agent is selected from the group consisting of antisense nucleic acids to a gene encoding a polypeptide comprising at least one of the sequences of SEQ ID NOs: 1 and 2, a gene encoding a polypeptide comprising an amino acid sequence having at least 25% homology to a sequence selected from the group consisting of SEQ ID NOs. 7-14, a gene encoding a polypeptide comprising an amino acid sequence having at least 50% homology to a sequence selected from the group consisting of SEQ ID NOs. 7-14, and a gene encoding a polypeptide comprising an amino acid sequence having at least 80% homology to a sequence selected from the group consisting of SEQ ID NOs. 7-14.

30 55. The agent of Claim 48, wherein said agent is selected from the group consisting of small molecules and drugs.

56. The agent of Claim 48, wherein said agent is for administration to an individual having a level of adipoQ or ApM1 activity which is above normal.

35 57. A method for determining whether an obese individual is at risk of suffering from a condition selected from the group consisting of a condition associated with a lower than desirable level of partitioning of dietary

lipids to the liver, obesity-related atherosclerosis, obesity-related insulin resistance, obesity-related hypertension, microangiopathic lesions resulting from obesity-related Type II diabetes, ocular lesions caused by microangiopathy in obese subjects with Type II diabetes, and renal lesions caused by microangiopathy in obese subjects with Type II diabetes, comprising the step of determining whether the individual has a lower than normal level of adipoQ activity, ApM1 activity, or activity of a compound analogous thereto.

58. A method for increasing the partitioning of dietary lipids to the liver comprising administering an agent which increases the activity of a compound selected from the group consisting of adipoQ, ApM1, C1q, compounds analogous to C1q, compounds comprising at least one sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:2, compounds comprising an amino acid sequence having at least 25% homology to a sequence selected from the group consisting of SEQ ID NOs. 7-14, compounds comprising an amino acid sequence having at least 50% homology to a sequence selected from the group consisting of SEQ ID NOs. 7-14, and compounds comprising an amino acid sequence having at least 80% homology to a sequence selected from the group consisting of SEQ ID NOs. 7-14 to an individual.

59. The method of Claim 58, wherein said individual suffers from a condition selected from the group consisting of obesity, obesity-related atherosclerosis, obesity-related insulin resistance, obesity-related hypertension, microangiopathic lesions resulting from obesity-related Type II diabetes, ocular lesions caused by microangiopathy in obese subjects with Type II diabetes, and renal lesions caused by microangiopathy in obese subjects with Type II diabetes.

60. The method of Claim 58, wherein said agent is selected from the group consisting of a derivative of adipoQ, ApM1 or an analogous compound which exhibits greater activity than the corresponding wild type protein, nucleic acids encoding adipoQ, ApM1, or an analogous compound, fragments thereof, and nucleic acids encoding a derivative of adipoQ, ApM1, or an analogous compound having greater activity than the corresponding wild type protein, and fragments thereof.

61. The method of Claim 58, wherein said agent is administered if it is determined that the level of ApM1, or an analogous protein in said individual is below normal.

62. A method for decreasing the partitioning of dietary lipids to the liver comprising administering an agent which decreases the activity of a compound selected from the group consisting of adipoQ, ApM1, C1q, compounds analogous to C1q, compounds comprising at least one sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:2, compounds comprising an amino acid sequence having at least 25% homology to a sequence selected from the group consisting of SEQ ID NOs. 7-14, compounds comprising an amino acid sequence having at least 50% homology to a sequence selected from the group consisting of SEQ ID NOs. 7-14, and compounds comprising an amino acid sequence having at least 80% homology to a sequence selected from the group consisting of SEQ ID NOs. 7-14 to an individual.

63. The method of Claim 62, wherein said individual suffers from a condition selected from the group consisting of cachexia in subjects with neoplastic or para-neoplastic syndrome or eating disorders.

64. The method of Claim 62, wherein said agent is selected from the group consisting of an antibody

which binds adipoQ, ApM1, C1q or an analogous protein, a derivative of adipoQ, C1qa, C1qb, C1qc, mul, cer, ApM1, or acrp which inhibits the activity of wild type adipoQ or wild type ApM1, a fragment of said derivative, antisense nucleic acids to the adipoQ gene, the ApM1 gene or a portion thereof, nucleic acids capable of forming a triple helix with a portion of the adipoQ gene or the ApM1 gene, and antibodies capable of binding the γ subunit, the C1q receptor (gC1q-R) or a protein related thereto.

65. The method of Claim 62, wherein said agent is administered if it is determined that the level of adipoq, ApM1, or an analogous protein in said individual is above normal.

66. A method of identifying a candidate compound for regulating the partitioning of dietary lipids between the liver and the adipose tissue comprising the steps of :

contacting the γ subunit, the C1q receptor (gC1q-R) a protein related thereto, or a fragment thereof with one or more molecules to be tested for binding activity under conditions which permit specific binding of said molecule to said γ subunit, C1q receptor (gC1q-R), protein related thereto, or fragment thereof; and

determining whether said one or more molecules bind to said γ subunit, C1q receptor (gC1q-R), protein related thereto, or fragment thereof .

67. The method of Claim 66, wherein said contacting step is performed using a cell expressing said γ subunit, C1q receptor (gC1q-R), protein related thereto, or fragment thereof.

68. The method of Claim 66, wherein said γ subunit, C1q receptor (gC1q-R), protein related thereto, or fragment thereof is immobilized on a support.

69. The method of Claim 66, further comprising contacting said γ subunit, C1q receptor (gC1q-R), protein related thereto, or fragment thereof with a known ligand and determining the ability of said one or more molecules to be tested for binding activity to compete with said known ligand for binding to said γ subunit, C1q receptor (gC1q-R), protein related thereto, or fragment thereof.

70. The method of Claim 66, wherein said molecule to be tested for binding to said γ subunit, C1q receptor (gC1q-R), protein related thereto, or fragment thereof is selected from the group consisting of polypeptides, peptides, derivatives or analogs thereof, drugs, and small molecules.

71. A method of identifying candidate pharmaceutical agents for reducing plasma triglyceride levels in an animal, comprising the steps of:

administering a test compound to a test animal; and

measuring a post-treatment level of plasma triglycerides in a blood sample obtained from the test

animal.